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Epidemiology and Control of Bancroftian Filariasis in Some Villages of Nagasaki Prefecture

3. Epidemiology and mass treatment of filariasis in Amakubo village *

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長崎県下の数部落に於けるフイラリア症の疫学と治療に関する研究. 3. 天久保部落に於けるフイラリア症の疫学と集団治療. 永友勇夫, 長崎大学風土病研究所衛生動物学研究室, 自衛隊札幌地区病院.

Introduction

In a farm village of 112 houses with about 630 people and highly endemic in filariasis for Japan, filaria control experiment with Hetrazan was made, without making mosquito control, during from October, 1953 to February, 1955.

Prior to and during the control experiment all-people surveys for microfilariae were made three times at a interval of four and a half months, and epidemiological considerations will be made from the data of the surveys.

For treatment the following dosage schedules of diethylcarbamazine were used: 2mg per kg of body weight three times a day for consecutive ten days ($2\times3\times10$), $2\times3\times15$ or $3\times3\times10$. By these large-dosage, 45 of all positives became negative by one course, 46 by two courses and 7, 1, and 1 by three, four, and five courses. On the effects and reactions of the drugs, detailed accounts will be reported here.

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Place and Method

The village where the control experiment of Bancroftian filariasis was made is situated at the northern extremity of the Nishisonoki peninsula, outside the Sasebo harbour, Nagasaki prefecture. The village lies in from seashore to hill-side and villagers are engaging in agriculture especially in growing vegetables. Accordingly, there are many fertilizer pits and jars near houses and in the field which are the most faborable breeding places of ***Culex pipiens pallens***, the most dangerous vector mosquito of the filariasis. This seems to be the reason why this village was found to be extraordinarily high in endemicity of filariasis among the neighboring villages in the preliminary survey

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made two months before the Commencement of this control experiment. The number of families in the village was 112 at the beginning but decreased to 109 by the close of the experiment. The population was about 630 but fluctuated time to time of blood examination and by the end of the experiment, among original microfilarial positives three persons were dead and six moved out from the village.

Blood examination for microfilariae was made taking three thick films amounting to about 20mm³ of blood from the ear-lobe of persons on a slide at night from 9 to 12 p.m., staining on the next day with dilute Giemsa's solution and examining them by binocular microscope. Usually 20mm³ of blood was taken but occasionally 40 or 60mm³ were smeared making three thick films on each of two or three slides. In the latter cases the mean numbers of microfilariae for 20mm³ were shown in the table and then the following expressions were given in the table: (40mm³/2) or (60mm³/3). On October 12-14, 1953, the 1st blood surrey for all persons in the village was performed. The 2nd and 3rd ones were made on March 1-2, 1954 and on July 9-11 of the same year. After each of these all-people surveys, microfilarial positives were only treated and examined for filariae again and again till all of them became negative.

The drug used in this control experiment was diethylcarbamazine (Hetrazan). The dosage schedules or the courses of the drug were as follows: 2mg per kg of body weight three times a day for consecutive ten days (=2×3×10), 2×3×15, or 3×3×10.

The special features of this control experiment are that no control measures were applied against the vector mosquitoes and that blood surveys for all people were made three times at a interval of about four and a half months and microfilarial positives found in these surveys were repeatedly treated by the large-dosage schedules.

Epidemiology of filariasis in the village

1. Clinical manifestations

The 1st filaria survey for all people in the

Table 1 Complaint of clinical manifestations made by 10 persons among 109 microfilarial positives

Clinical manifestation	No. person, age & sex	
	No.	Age and sex
History of fever	6	40♂, 58♂, 60♂, 61♂, 37♀, 72♀,
History of lymphangitis	1	65♂
History of chyluria	1	20♂
Hydrocele	1	78♂
Slight elephantiasis	1	60♀

Table 2 Analysis of blood survey in Amakubo village before mass treatment with Hetrazan

Level of Mf counts	No. of Mf counts at each level	Persons examined		No. of Mf	
		No.	%	Total	Mean
A. Result of the first survey made on October 12-14, 1953					
1- 5	1:12; 2:11; 3:11; 4:5; 5:4	43	6.9	107	2.5
6- 10	6:4; 7:5; 8:3; 9:4; 10:1	17	2.7	129	7.6
11- 30	11:6; 12:1; 14:3; 15:3; 16:4; 17:1; 19:2; 20:2; 21:1; 22:1; 26:2	26	4.2	419	16.1
31- 50	50:1	1	0.2	50	50.0
51-100	63:1; 76:1; 81:1	3	0.5	220	73.3
100+	125:1; 151:1	2	0.3	276	138.0
Positives found in the first survey		92	14.8	1201	13.1

B. Newly found positives at the second survey made on March 1-2, 1954

1- 5	1 : 2 ; 2 : 2 ; 3 : 3	7	1.1	15	2.1
6- 10	6 : 1 ; 9 : 1	2	0.3	15	7.5
11- 30	14 : 1	1	0.2	14	14.0
31- 50	37 : 1	1	0.2	37	37.0
	Positives found in the second survey	11	1.8	81	7.4

C. Newly found positives at the third survey made on July 9-11, 1954

1- 5	0.5 : 2 ; 1.5 : 1 ; 2.0 : 2 ; 2.5 : 1	6	1.0	9	1.5
	Total persons positive	109	17.5	1291	11.8
0	Throughout the above surveys	513	82.5	0	0
	Total persons	622	100.0		2.1

Remarks: 1) 20mm³ of peripheral blood was examined for microfilariae(Mf) in the first and second surveys while in the third survey 40mm³ was examined and the mean by 20mm³ was given in the table.
2) This table was compiled on the base of the size of population of this village at the time of the third survey, as the size of population varied a little with the time of the survey.
3) Between the mean number (13,054) of Mf at the 1st survey and that (5,294) of Mf at the 2nd and 3rd surveys, significant difference is attained at 5% level

village was performed on October 12-14, 1953 and it was found that the village was highly endemic for Japan but that clinical manifestations complained of by villages were rather few in case and light in degree as shown in Table 1.

2. Percentage of people positive and microfilarial density

Microfilarial count per 20mm³ made at each level, the number and percentage of persons positive, and the average number of microfilariae per positive person are tabulated in Table 2. In the 1st blood survey, 92 persons were found positive who were administered with Hetrazan (cf. Table 10) and examined repeatedly for microfilariae. Four and a half months later the 2nd survey for all people was made and when 11 persons were newly found to be positive. Those who were remaining still positive and who were found positive in the 2nd survey were administered with the drug. In the 3rd survey made four and a half months later from the 2nd one, 6 persons were again newly found to be positive. Persons being still positive and being newly found positive were similarily administered and examined for microfilariae.

Table 2 shows that the persons having smaller number of microfilariae are very large in number, especially so with persons having 1-5 counts, and that the average number of microfilariae per positive person found in the 1st survey is significantly higher than that of those found in the 2nd and 3rd surveys.

The reason why the microfilarial counts of the newly found positives were significantly low, as also shown in Table 3, appears to be due to

Table 3 Age and No. of Mf per 20mm³ of newly found positives

in the 2nd survey				in the 3rd survey			
Male		Female		Male		Female	
Age	No. Mf	Age	No. Mf	Age	No. Mf	Age	No. Mf
5	1	13	9	13	2.5	31	2.0
13	3	34	3	18	0.5	61	2.0
16	37	36	2	67	0.5	84	1.5
24	1	58	2	—	—	—	—
41	14	—	—	—	—	—	—
46	3	—	—	—	—	—	—
79	6	—	—	—	—	—	—

the counts were being probably small in some persons whose counts were so small and irregular in number in 20mm³ of blood as to be oversighted in the previous survey, and in some others who became positive for the first time after the previous survey.

3. Number of positives and microfilarial density by age group and sex

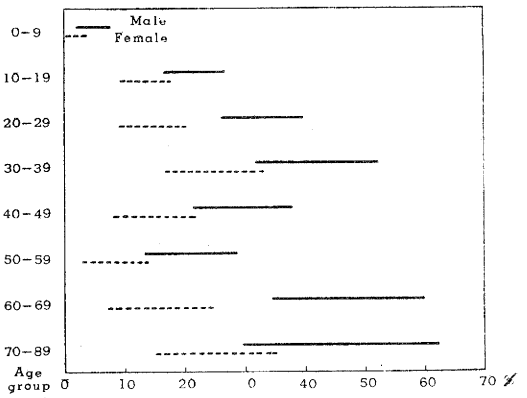
Throughout the all-people surveys made three times, 109 persons were detected to be positive for microfilariae. The youngest positive was a boy of 5 years old with only 1 microfilaria in 20mm³ of blood. The oldest one was 84 aged woman with 3 microfilariae in 40mm³ of her blood.

The number of positives by age group and sex are tabulated in Table 4. To examine whether there are special differences in the percentage positive among persons of different age groups and sexes, comparison of percentages are made in 60% confidence intervals of population percentages as illustrated in Fig. 1. The percentage positive become higher with advance in age group reaching a peak in 30-39 group, decreasing in 50-59 group and again increasing markedly towards the oldest age group. The reason of decrease in 40-49 and especially in 50-59 age group is uncertain but is thought to be presumably due to the infection was being intense in old years decreasing for some twenty years and then again becoming active in recent years.

Table 4 Numbers of positives for microfilariae by age group and sex

Age group	Male		Female	
	Persons examined	Persons positive	Persons examined	Persons positive
0- 9	72	3	74	1
10-19	61	13	68	9
20-29	46	15	43	6
30-39	24	10	44	10
40-49	31	9	29	4
50-59	30	6	30	2
60-69	17	8	21	3
70-89	11	5	21	5
Total	292	69	330	40

Fig. 1 60% confidence intervals of population percentage numbers of persons positive for microfilariae for the percentage numbers of positives by age group and sex



The state of distribution in percentage positive is nearly similar with both sexes but the percentages are fairly remarkably lower in every group in female especially in those of 20-29 and 60-69. The higher percentage in male is probably due partly to the more frequent exposure to the vector mosquitoes and partly to the custom of the youth in the village to spend only the night by group in each fixed club house scarcely using mosquito net.

Fig. 2 60% confidence intervals of population means for the mean number of microfilariae by age group

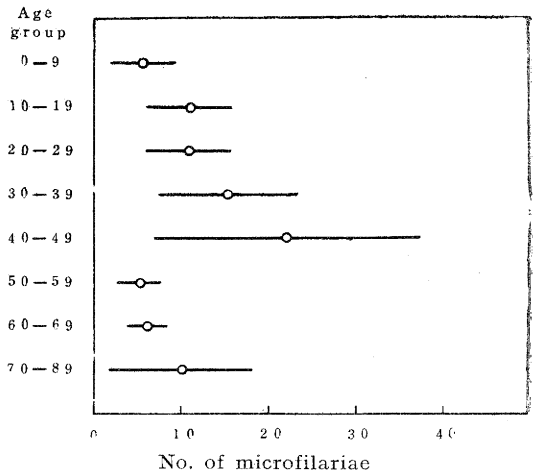


Table 5 Mean numbers of microfilariae by sex

Sex	No. of positives	No. of micorfilariae	
		Total	Mean *
Male	69	977.5	14.17
Female	39	312.0	8.00

* Between the two means no significant difference is attained at 5% level

It is of special interest to say that among the population mean numbers of microfilariae or microfilarial densities by age group, no significant differences are attainable, although the sample means which are shown by small circles in the figure (Fig. 2) are seen at a glance to differ markedly. It is also of interest that the difference between the mean number of microfilariae by sex is not significant as shown in Table 5.

The fact that although there are significant differences among the percentage positive by age group and sex, among the mean numbers of microfilariae there are no significant differences, may be explained by the occurrence of a great variation to which individual microfilarial counts are subjected. This in turn, suggests that in every age group, even in those of being higher in percentage positive and also in both sexes, new filarial infection have been prevailing in recent years in this village.

Table 6 Number of families having various numbers of positives

Time of survey	Persons positive	No. of positives in a family					Total no. of positives
		1	2	3	4	5	
1st survey	92	28	10	9	3	1	51
2nd survey	103	27	11	11	4	1	54
3rd survey	109	26	10	14	4	1	55

Remark : The 1st, 2nd, and 3rd surveys were made on Oct. 12-14, 1953, March 1-2, and July 9-11, 1954 respectively

4. Family infection

As mentioned above, in the first survey 92 positives were detected and in the 2nd and 3rd ones 11 and 6 positives were newly found respectively but the numbers of families having positives in various numbers were, as shown in Table 6, 51, 54, and 55 in total respectively. The more detailed account is shown in Table 7 in which the size of families involved in this village and the number of families having zero and various numbers of positives at each family

Table 7 Showing the frequency distribution of the number of families having various numbers of positives at each family size, together with the number of persons examined, positives, and percentage positive

Size of family	No. of positives in a family						Total families	Persons examined	Persons positive	% positive
	0	1	2	3	4	5				
1	1	—	—	—	—	—	1	1	—	
2	8	—	2	—	—	—	10	20	4	
3	6	3	—	—	—	—	9	27	3	
4	7	4	1	—	—	—	12	48	6	
5	10	1	2	2	—	—	15	75	11	
6	10	9	—	3	1	—	23	138	22	
7	4	3	1	1	—	—	9	63	8	
8	2	2	1	5	1	1	12	96	28	
9	3	3	2	3	2	—	13	117	24	
10	3	1	1	—	—	—	5	50	3	
Total	54	26	10	14	4	1	109	635	109	17.17

Table 8 Hypothetical numbers of families having various number of positives at each family size, calculated under the assumption of binomial distribution with P=17.17%, that is, the percentage positive for microfilariae in the village

Size of family	No. of positives in a family								Total families
	0	1	2	3	4	5	6	7	
1	0.828	0.172	—	—	—	—	—	—	1.000
2	6.861	2.845	0.295	—	—	—	—	—	10.001
3	5.115	3.181	0.660	0.046	—	—	—	—	9.002
4	5.648	4.684	1.457	0.202	0.011	—	—	—	12.002
5	5.849	6.062	2.514	0.521	0.054	0.002	—	—	15.002
6	7.427	9.237	4.789	1.323	0.205	0.016	0.000	—	22.997
7	2.408	3.494	2.173	0.751	0.156	0.020	0.001	0.000	9.003
8	2.659	4.410	3.200	1.327	0.343	0.056	0.006	0.000	12.001
9	2.386	4.451	3.691	1.785	0.555	0.116	0.016	0.001	13.001
10	0.760	1.576	1.470	0.813	0.295	0.074	0.013	0.002	5.003
Total families	39.941	40.112	20.249	6.768	1.619	0.284	0.036	0.003	109.012

size are given.

When supposed the chance of infection of filariasis would have been uniformly distributed for all individuals at a rate of 17.17% i.e. the percentage positive of the village, the frequency distribution of the number of families having various numbers of positives at each family size is thought to follow a binomial distribution. Then hypothetical frequencies in binomial distribution with p=17.17% at each family size are calculated as shown in Table 8.

Comparing the observed frequencies with the hypothetical ones, we can test the homogeneity of the former as assumed to be a random sample from binomial from. The test was made in Table 9 the result of which shows that the observed frequency distribution can not be said as a random drawing sample from binomial distribution with p=17.17%. In other words, the population distribution for the observed one may not be binomial. From the above result, considering the states of observed frequencies of the number of families, we arrived at a conclusion that a fairly intense family infection of filariasis were occuring in this village.

This may due to such habits of ***Culex pipiens pallens***, the most important and the only vector mosquito of the disease in the district, as its being presumably very short in flight range, being very fond of human blood, and being partial in selecting its breeding place near the house as suggested by the author in the former reports.

Table 9 Test of homogeneity of the number of families in a distribution of the binomial form

No. of positives in a family	0	1	2	⩾3	Total
Observed No. of families	54	26	10	19	109
Hypothetical No. families	39.94	40.11	20.25	8.71	109.01
Deviation	14.06	-14.11	-10.25	10.29	-0.01
(Deviation)^2	197.68	199.09	105.06	105.88	
$\frac{(\text{Deviation})^2}{\text{Hypothetical}}$	4.949	4.964	5.188	12.156	$X^2=27.257$ Df=2, P<0.001

Treatment with Hetrazan

1. Treatment

The detailed accounts of blood examinations and drug administrations are show in Table 10. The administration of diethylcarbamazine was applied only to the 100 positives excluding 9 ones who were dead or moved out from the village during the experiment. The details are given in Table 11.

The number of microfilariae per positive

Table 10 Result of blood examination and drug administration
(Unless otherwise stated, blood examination was made with 20mm³)

Date	Blood survey for all persons (3 times), for only positives (11 times) and drug administration (D.1, D.2···D.6)	Number of persons					Total no. Mf	No. Mf per positive
		not at home	dead or moving out	treated	examined for Mf	found positive		
Oct.12-14,1953	1st blood survey for all persons (629)	—	—	—	629	92	1201	13.1
Nov.2-11	Diethylcarbamazine administration : D.1	—	—	92	—	—	—	—
Nov. 7	Blood examination for persons found positive at the 1st survey (B.E. for+)	4	1	—	87	27	98	3.6
Nov.14	B. E. for +	—	1	—	91	31	95	3.1
Nov.28	B. E. for +	—	2	—	90	27	73	2.7
Dec. 12	B. E. (60mm³/3) for +	4	2	—	86	50	120	2.4
Jan. 9, 1954	Diethylcarbam. administ. : D.2	—	—	25	—	—	—	—
Jan. 23	B. E. for +	4	3	—	85	18	32	1.8
Mar. 1-2	2nd blood survey for all persons(634) — B. E. for + at 1st survey (1)	1	3	—	88	22	43	2.0
	2nd blood survey for all persons(634) — Others (2)	—	—	—	546	11	81	7.4
Apr. 3	B. E. for + — at the 1st survey (1)	2	3	—	87	17	48	2.8
	B. E. for + — at the 2nd survey (2)	—	—	—	11	9	67	7.4
Apr. 23	Diethylcarbam. administ. : D.3 to positives — found at 1st survey(1)	—	—	17	—	—	—	—
	Diethylcarbam. administ. : D.3 to positives — found at 2nd survey(2)	—	—	8	—	—	—	—
May 9	B. E. (60mm³/3) for + (1)	1	4	—	87	16	34.2	2.1
	B. E. (60mm³/3) for + (2)	—	—	—	11	3	31.0	10.3
May 10	Diethylcarbam. administ. : D.4 to (1)	—	—	14	—	—	—	—
	Diethylcarbam. administ. : D.4 to (2)	—	—	3	—	—	—	—
May 31	B. E. for + (1)	4	5	—	83	4	8	2.0
	B. E. for + (2)	2	—	—	9	0	0	0
Jul.9-11	3rd blood survey (40mm³/2) for all persons (622) — B. E. for+(1)	—	6	—	86	3	1.5	0.5
	3rd blood survey (40mm³/2) for all persons (622) — B. E. for+(2)	—	—	—	11	3	3.5	1.2
	3rd blood survey (40mm³/2) for all persons (622) — Others (3)	—	—	—	525	6	9.0	1.5
Sept. 28	Diethylcarbam. administ. : D.5 to (1)	—	—	6	—	—	—	—
	Diethylcarbam. administ. : D.5 to (2)	—	—	3	—	—	—	—
	Diethylcarbam. administ. : D.5 to (3)	—	—	5	—	—	—	—
Oct. 10	B. E. + for (1)	—	7	—	85	4	10	2.5
	B. E. + for (2)	—	1	—	10	1	1	1.0
	B. E. + for (3)	—	1	—	5	0	0	0
Dec. 13	B. E. (60mm³/3) for + (1)	—	7	—	85	1	4.7	4.7
	B. E. (60mm³/3) for + (2)	—	1	—	10	1	0.7	0.7
	B. E. (60mm³/3) for + (3)	—	1	—	5	0	0	0
Feb. 5, 1955	Diethylcarbam. administ. : D.6 to (1)	—	—	4	—	—	—	—
	Diethylcarbam. administ. : D.6 to (2)	—	—	1	—	—	—	—
Feb. 28	B. E. for + (1)	—	7	—	85	0	0	0
	B. E. for + (2)	—	1	—	10	0	0	0
	B. E. for + (3)	—	1	—	5	0	0	0

Table 11 Relation between the number of courses of Hetrazan and the number of carriers became negative for microfilariae

(Out of 109 carriers, 9 ones were dead or moved out during the control period as shown in Table 8, and 100 positives were treated with satisfactory results)

No. of courses of drug required to make negative	No. of carriers became negative		Dosage (mg per kg)*	
	No.	Total	Schedule	Total
1	33	45	2×3×10	60
	7		2×3×15	90
	5		3×3×10	90
2	27	46	2×3×10+2×3×15	150
	15		2×3×10+3×3×10	150
	2		2×3×15+3×3×10	180
	1		(1+1+2)×15+2×3×15	150
	1		(1×3×1+0.5×3×12)+1×3×15	66
3	2	7	2×3×10+2×3×15+2×3×10	210
	1		2×3×10+3×3×10+2×3×10	210
	1		2×3×10+3×3×10+2×3×15	240
	1		2×3×10+3×3×10+3×3×10	240
	1		2×3×10+2×3×15+3×3×10	240
	1		2×3×15+3×3×10+2×3×10	240
4	1	1	2×3×10+3×3×10+2×3×15+2×3×10	270
5	1	1	2×3×10+3×3×10+2×3×15+3×3×10+2×3×10	390

* A dosage : For instance, 2mg per kg of body weight three times a day for consecutive 10 days is represented by a expression : 2×3×10.

abruptly decreased in number already on the fifth day after the start of the administration of Hetrazan. Thereafter, however, the number not necessarily decreased remarkably. The percentage number of positives decreased very gradually with repetition of drug administration fluctuating, however, time to time especially when the microfilarial counts became very small, and in cases of 40 or 60mm³ of blood being examined.

Out of 92, 11, and 6 positives found in the 1st, 2nd, and 3rd all-people surveys, 7, 1, and 1 persons were dead or moved out from the village and therefore 85, 10, and 5 positives were treated till their blood became entirely negative for microfilariae. Of 85 positives 33, 44, 6, 1, and 1 ones became negative by one, two, three, four, and five courses of drug administrations. Of 10 positives newly found in the 2nd survey, 7, 2, and 1 ones became negative by one, two, and three courses. Five positives found newly at the 3rd survey became all negative by one course. Thus 45 (45%) positives became negative for microfilariae by one course of drug, 46 (46%) became negative by two courses, and 7, 1, and 1 by three, four, and five courses as shown in Table 11. Among those who treated repeatedly, several persons became negative hardly on the last or the last but one times of blood examination. Although these persons and perhaps some others having turned to nagative more easily, can not be necessarily regarded as completely cured of the disease, the control experiment was closed with success in becoming all negative at least once, sixteen and a half months after the institution.

At any rate, it is noteworthy fact that even by such large doses as used in this control experiment, only 45% of positives turned negative by one course and 46% did by two courses and that 9% did barely by three to five courses. It is also noteworthy that in the 2nd and 3rd

Table 12 Comparison between sexes in number of becoming negative by one course of Hetrazan and two to five courses of the drug

No. courses of drug	Male	Female	Total
No. carriers who became negative by one course of Hetrazan	35	15	50
No. carriers who became negative by two to five courses of Hetrazan	34	24	58
Total	69	39	108

Result of x^2 test $x_s^2=1.45$ Df=1 20%<p<30%

Table 13 Comparison among age groups in number of becoming negative by one course of Hetrazan and two to five courses of the drung

Age group	No. carriers became negative by one course of Hetrazan		by two to five ones of the drug	
0- 9	3	15	1	11
10-19	12		10	
20-29	8	16	13	25
30-39	8		12	
40-49	5	9	8	12
50-59	4		4	
60-69	7	10	4	10
70-79	3		6	
Total	50		58	

$x_s^2=2.44$ Df=3 30%<p<50%

Table 14 Comparison between the mean numbers of microfilariae of carriers who became negative by one course of Hetrazan and two to five courses of the drug

Items	No. persons	Original No. Mf	
		Total	Mean
Carriers who became negative by one course of Hetrazan	50	275.5	5.51 *
Cariers who became negative by two to five courses of Hetrazan	58	1014.0	17.48

* Between the two means, a significant difference is attained at 5% level

all-people survey, 11 and 6 persons were newly found to be positive and that 13 persons of these were in families having one or more carriers. These findings suggest the need of application of drug administration to all people regardless of their being positive or not by a rather small dose for a long period.

It is of interest to know whether the disease in more easily curable in one sex or in any age group, then the percentage numbers of persons becoming negative by one course and two to five courses are compared with sexes or age groups in Tables 12 and 13. From the results of x^2 test, however, it can not be said that neither one sex nor any age group are curable of the disease more easily than the other or others.

Next, it has been generally supposed that the

Table 15 Reactions observed at the first course of Hetrazan (2mg/kg×3 times×10 days)

Reactions	Days after the start of treatment					No. of cases	Duration in days of reaction				
	1	2	3	4	5		1	2	3	4	5
Headache	8	28	7	0	2	45	21	13	3	5	3
Fever	3	8	3	0	0	14	4	6	2	2	0
Lumbar pains	2	6	1	0	0	9	3	3	1	2	0
Abdominal pains	2	4	1	0	0	7	4	2	1	0	0
Lymphangitis	1	1	0	0	0	2	0	1	0	1	0
Lassitude etc.	4	9	3	2	0	18	10	2	3	3	0

Persons examined: 107, persons without reactions: 28, persons with any kind of reactions: 79

facility by which a positive turn to a negative state not necessarily depends on his microfilarial count. To acertain this, the mean number of microfilariae for positives who became negative by one course of Hetrazan is compared with that of those becoming negative by two to five courses. The result of a significance test between the two means shows there being significant difference. This means that, in general, the more heavily infected the less easily curable.

2. Reactions

By the usage of the large dosage, fairly severe reactions were observed at the first course of the drug as seen in Table 15. The reactions were complained of more severely on the second day of the drug administration and lasted mostly for two days.

Summary

1) Filaria control experiment was performed during from October, 1953 to February, 1955 in a farm village having 112 houses and about 630 people and highly endemic in filariasis for Japan, making all-people blood surveys three times at a interval of four and a half months, administering Hetrazan to positives, and examining their blood repeatedly till all positives turned to negative state.

2) The clinical manifestations of filariasis were rare and complaint of the history of them were few. The percentage positive for all people was 17.5%. The microfilarial density per 20mm^3 of blood for positives and for all people were 11.8 and 2.1 respectively. The youngest positive was a boy of 5 years old with one microfilaria and the oldest one was 84 aged woman with 2 microfilariae.

3) The percentage positive was very low in 0-9 age group increasing gradually and reaching a peak at 30-39, decreasing thereafter to 50-59 age group and again increasing towards the oldest group. The sexes were nearly similar in the trend of percentage distribution but clearly lower in female. However, there were no significant differences in the mean numbers of microfilariae between the sexes or age groups. The above appears to show that the infection of filariasis had been active in old years in this village decreasing for some twenty years and were prevailing again in recent years probably in every age group.

4) The occurrence of intense family infection of the disease is proved. The phenomenon seems to have close bearing on the habits of the domestic vector mosquito, ***Culex pipiens pallens***.

5) In the 1st all-people survey, 92 persons were found to be positive. In the 2nd and 3rd surveys 11 and 6 persons were newly found to be positive. Of these, 7, 1, and 1 were dead or moved out during the control experiment and therefore treatment was made with 100 persons.

6) Large-dosage schedules of diethylcarbamazine, 2mg per kg of body weight three times a day for consecutive ten days (=2×3×10), 2×3×15, or 3×3×10 were used. By these large dosages, only 45 out of 100 positives became negative by one course of administration, 46 positives became negative by two courses, and 9 ones became negative hardly by three to five courses.

7) Although there are no significant differences in curability among sexes or age groups, it can be clearly said, against the general suposition, that the more heavily infected with microfilariae the less easily curable.

8) The difficulty in detecting positives harboring extremely small number of microfilariae, the imposibility in finding persons being under incubation state, the difficulty in curing positives with much easy even by such large dosages as used in this experiment, and the severity in reactions caused by the usage of large dosage, all come into questions to be considered and improved hereafter.

Literatures

1) Abe, Y. and Yamashita, H.: Epidemiological studies on the filariasis due to *Wuchereria bancrofti*. 1. Observation on filarial infection in Kagoshima prefecture proper. Med. J. Ragoshima Univ., 7 (2) : 300-305, 1955. (In Japanese with English summary).

2) Baisas, F. E. : Notes on Philippine mosquitoes, XIX. The mosqtito problem in the control of filariasis in Sorsogon Province. Philip. J. Sci., 86 (1) : 71-120, 1957.

3) Edeson, J. F. B. and Wharton, R. H. : Studies on filariasis in Malaya. : Treatment of *Wuchereria malari*-carriers with monthly or weekly doses of diethylcarbamazine (Banocide). Ann. Trop. Med. Paras., 52(1) : 87-92, 1958.

4) Katamine, D., Yamasaki, T. and Yoshida, U. : Statistical and clinical observations on the endemicity of filariasis on islands in Nagasaki Ken. Nagasaki Igakkai Zassi, 27 (4): 185-194, 1952. (In Japanese with English summary).

5) Kessel, J. F., Thooris, G. C. and Bambridge, B. : The use of diethylcarbamazine (Hetranzan or Netezine) in Tahiti as an aid in the control of filariasis. Amer. J. Trop. Med. Hyg., 2 : 1050-1061, 1953.

6) Kessel, J. F. : An effective programme for the control of filariasis in Tahiti. Bull. Wld Hlth Org., 16 : 633-664, 1957.

7) Nagahana, M. : Epidemiology of filariasis in Kagoshima prefectere. X Summary, Consideration and Conclusion. Kagoshima Med. J., 30 (7-8) : 257-279, 1957. (In Japanese) .

8) Nagatomo, I. : Epidemiology and control of bancroftian filariasis in some villages of Nagasaki prefecture. 1. Incidence of filariasis and natural infection rate of mosquitoes in Nanatugama and Taira villages. Endemic Dis. Bull. Nagasaki Univ., 2 (4) : 296-306, 1960.

9) ———— : Epidemiology and control of bancroftian filariasis in some villages of Nagasaki prefecture. 2. Nocturnal feeding activities of mosquitoes in a filaria endemic section, Kamisikama of Nanatugama village. Endemic Dis. Bull. Nagasaki Univ., 2 (4) : 307-320, 1960.

10) Omori, N., Kamura, T., Fujisaki, T., Suenaga, O., Kitamura, S., Katamine, D., Era, E. and Fukamachi, H. : Filaria control experiments in western Kyushu, Japan. Jap. J. Paras., 8 (6) : 886-894, 1959. (In Japanese with English summary) .

11) Oshima, M. : Studies on the incidence of bancroftian filariasis and the natural infection of mosquitoes in western Kyushu, Japan. I. On the incidence of filariasis. Nagasaki Igakkai Zassi, 30 (11) : 1467-1477, 1955. (In Japanese with English summary) .

12) Poynton, J. O. and Hodgkin, E. P. : Endemic filariasis in the Federated Malay States. Bull. Inst. Med. Res. Federated Malay States. No. 1 of 1938.

13) Raghavan, N. G. S. : Epidemiology of filariasis in India. Bull. Wld Hlth Org., 16 : 553-579, 1957.

14) Rosen, L. : Observations of the epidemiology of human filariasis in French Oceania. Amer. J. Hyg., 61 : 219-248, 1955.

15) Wharton, R. H., Edeson. J. F. B., Wilson, T. and Reid, J. A. : Studies on filariasis in Malaya : pilot experiments in the control of filariasis due to *Wuchereria malayi* in East Pahang. Ann. Trop. Med. Paras. 52 (2) : 191-205, 1958.

総　　括

1) 長崎県西彼杵半島北端の天久保部落で1953年10月から1955年2月迄の16ケ月半の間に全員の採血を約4ケ月半置きに3回行い，1回目に92名，2回目に新たに11名，3回目に更に6名の仔虫保有者を発見し，仔虫保有者にはその都度 Diethylcarbamazine, 2mg/kg×1日3回×連続10日，2×3×15又は3×3×10等の大量投与を行つて採血と投与を繰返し全員を陰転させた，

2）仔虫保有率は年令層間に有意差があつて0—9才代では著しく低く，30—39代で一つの山を描き，50—59代で著減して，高令層間に向つて再び非常に高くなる．このように仔虫保有率は年令層間及び男女間に有意的な差がみられるが，平均仔虫数は何れの場合にも有意差は認められない．これは，保有仔虫数に著しい変異のある事によるものである．これらの事実は本部落では，古く高度に侵淫していた後に約20年間の低感染時代があり，その後最近数拾年間は各年令層及び男女を通じて新しい感染が起つている事を暗示するものゝようである．

3）本部落内での仔虫保有者の分布状況を調べた結果，明らかな家族集積性のある事が認められた．

4）上述の強力な投与量によつて治療した100名中45，46，7，1及び1名は夫々1，2，3，4及び5回の治療によつて仔虫の陰転をみた．

5）1回の治療で陰転した45名と2回以上で陰転した55名について年令層別及び性別に百分比を比較すると年令間及び男女間に陰転の難易は認められない．然し，45名と55名の平均仔虫数間には有意差があつて仔虫数の少ないものが陰転し易い事を示す．

6）仔虫数の非常に少ない場合には発見が不確実であり特に20mm³の検血によつては発見出来ない場合のあること，潜伏期間中の患者の発見は現在不可能であること，本実験で使用したような大量投与によつても1回の治療によつて尚45%の陰転を見るのみで，人によつては4回又は5回の大量，長期の治療が必要であること，大量投与によつて可成り著しい副作用がみられる等のことを考え合せると，比較的少量を仔虫の有無に拘らず侵淫部落の全員に，長期に亘つて間隔投与する事が有利であると考えられる．

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